

PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

| | |
|---|---|
| Date of mailing (day/month/year) 09 December 1999 (09.12.99) | |
| International application No. PCT/US99/07854 | Applicant's or agent's file reference UNMC 63124PCT |
| International filing date (day/month/year) 09 April 1999 (09.04.99) | Priority date (day/month/year) 09 April 1998 (09.04.98) |
| Applicant TRACY, Steven, M. et al | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
03 November 1999 (03.11.99)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

| | |
|--|--|
| <p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p> | <p>Authorized officer Carlos Naranjo</p> <p>Telephone No.: (41-22) 338.83.38</p> |
|--|--|

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| DK | Denmark | LR | Liberia | SG | Singapore | | |
| EE | Estonia | | | | | | |

INTERNATIONAL SEARCH REPORT

 International application No.
 PCT/US99/07854

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : C12N 7/02, 15/00, 9/12, 7/00, 15/00; C07H 21/02, 21/04

US CL : 435/239, 172.3, 194, 235.1, 320.1; 536/23.1, 23.7

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/239, 172.3, 194, 235.1, 320.1; 536/23.1, 23.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| Y | LEE et al. Genomic Regions of Cocksackie virus B3 Associated with Cardiovirulence. J. Med. Virol. 1997. Vol. 52. pages 341-347. | 1-30 |
| Y,P | US 5,869,036 A (BELSHE et al) 23 February 1999, see entire document. | 1-30 |
| Y | ZHANG et al. Attenuation of a Reactivated Cardiovirulent Cocksackievirus B3: The 5'-Nontranslated Region Does Not Contain Major Attenuation Determinants. J. Med. Virol. 1993. 41. pages 129-137, see entire document. | 1-30 |

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

| | |
|---|--|
| * Special categories of cited documents: | *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| *A* document defining the general state of the art which is not considered to be of particular relevance | *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
| *E* earlier document published on or after the international filing date | *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | *A* document member of the same patent family |
| *O* document referring to an oral disclosure, use, exhibition or other means | |
| *P* document published prior to the international filing date but later than the priority date claimed | |

Date of the actual completion of the international search

23 MAY 1999

Date of mailing of the international search report

02 JUN 1999

 Name and mailing address of the ISA/US
 Commissioner of Patents and Trademarks
 Box PCT
 Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

JENNIFER GRASER

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/07854

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| Y | ZHANG et al. Cocksackievirus B3-Induced Myocarditis-Characterization of Stable Attenuated Variants that Protect Against Infection with the Cardiovirulent Wild-Type Strain. Am. J. Ped. June 1997. Vol. 150. No. 6. pages 2197-2207, see entire document. | 1-30 — |
| A | RAMSINGHI et al. A Point Mutation in the VP4 Coding Sequence of Cocksackievirus B4 Influences Virulence. J. Virol. November 1995. Vol. 69. No. 11. pages 7278-7281, see entire document. | 1-30 |
| A | BOWLES et al. Detection of Cocksackie-B-Virus-Specific RNA Sequences in Myocardial Biopsy Samples From Patients With Myocarditis and Dilated Cardiomyopathy. The Lancet. May 1986. pages 1120-1122, see entire document. | 1-30 |

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/07854

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, DIALOG, ALLSCIENCE

search terms: attenuat?, rna-dependent polymerase?, dna polymerase?, virus genome, viral vector?, enterovirus, cocksackievirus, pol (1w) gene

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

09/6479111

REC'D 28 FEB 2000

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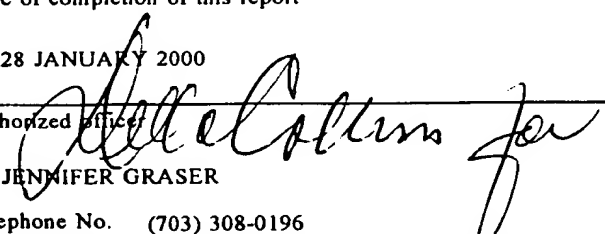
(PCT Article 36 and Rule 70)

| | | |
|--|---|---|
| Applicant's or agent's file reference UNMC 63124PCT | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/US99/07854 | International filing date (day/month/year) 09 APRIL 1999 | Priority date (day/month/year) 09 APRIL 1998 |
| International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet. | | |
| Applicant UNIVERSITY OF NEBRASKA BOARD OF REGENTS | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

| | |
|--|---|
| Date of submission of the demand 03 NOVEMBER 1999 | Date of completion of this report 28 JANUARY 2000 |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 | Authorized officer  JENNIFER GRASER |
| Facsimile No. (703) 305-3230 | Telephone No. (703) 308-0196 |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/07854

I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

☒ the international application as originally filed.

☒ the description, pages 1-23 , as originally filed.

pages NONE , filed with the demand.

pages NONE , filed with the letter of _____

pages _____ , filed with the letter of _____

☒ the claims, Nos. 1-30 , as originally filed.

Nos. NONE , as amended under Article 19.

Nos. NONE , filed with the demand.

Nos. NONE , filed with the letter of _____

Nos. _____ , filed with the letter of _____

☒ the drawings, sheets/~~fig~~ 0 , as originally filed.

sheets/~~fig~~ NONE , filed with the demand.

sheets/~~fig~~ NONE , filed with the letter of _____

sheets/~~fig~~ _____ , filed with the letter of _____

2. The amendments have resulted in the cancellation of:

☒ the description, pages NONE .

☒ the claims, Nos. NONE .

☒ the drawings, sheets/~~fig~~ NONE .

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/07854

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

| | | |
|-------------------------------|--------------------|-----|
| Novelty (N) | Claims <u>1-30</u> | YES |
| | Claims <u>NONE</u> | NO |
| Inventive Step (IS) | Claims <u>1-30</u> | YES |
| | Claims <u>NONE</u> | NO |
| Industrial Applicability (IA) | Claims <u>1-30</u> | YES |
| | Claims <u>NONE</u> | NO |

2. CITATIONS AND EXPLANATIONS

Claims 1-30 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a modified virus genome which has at least one *pol* gene modification which results in a decreased reversion rate from attenuated virus to non-attenuated virus as compared to an equivalent virus genome without the *pol* gene modification.

----- NEW CITATIONS -----

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/07854

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

Int. Cl. (6): C12N 7/02, 15/00, 9/12, 7/00, 15/00; C07H 21/02, 21/04 and US Cl.: 435.239, 172.3, 194, 235.1, 320.1; 536/23.1, 23.7

PATENT COOPERATION TREATY

WO 99/53034
PCT/US99/07854

09/647911

PCT

From the INTERNATIONAL BUREAU

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

REED, Janet, E.
Dann, Dorfman, Herrell and Skillman
Suite 720
1601 Market Street
Philadelphia, PA 19103
ÉTATS-UNIS D'AMÉRIQUE

| | | |
|--|--|--|
| Date of mailing (day/month/year) 21 October 1999 (21.10.99) | | |
| Applicant's or agent's file reference UNMC 63124PCT | | IMPORTANT NOTICE |
| International application No. PCT/US99/07854 | International filing date (day/month/year) 09 April 1999 (09.04.99) | Priority date (day/month/year) 09 April 1998 (09.04.98) |
| Applicant UNIVERSITY OF NEBRASKA BOARD OF REGENTS et al | | |

- Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU,CN,EP,IL,JP,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

- The following designated Offices have waived the requirement for such a communication at this time:

AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,ES,FI,GB,GD,GE,GH,GM,HR,
HU,ID,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,
SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZA,ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

- Enclosed with this Notice is a copy of the international application as published by the International Bureau on
21 October 1999 (21.10.99) under No. WO 99/53034

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

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|--|------------------------------------|
| The International Bureau of WIPO 34, chemin des Colmbettes 1211 Geneva 20, Switzerland | Authorized officer J. Zahra |
| Facsimile No. (41-22) 740.14.35 | Telephone No. (41-22) 338.83.38 |